Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the amendments and remarks presented herein, is respectfully requested. Claims 1 and 22 are amended, and claims 23-30 are added. Claims 1-3 and 22-30 are pending. The amendments to the claims are intended to clarify Applicant's invention and not intended to limit the equivalents to which any claim element may be entitled.

The present application is a continuation-in-part application of U.S. application Serial No. 07/922,996, filed on July 30, 1992, which is a continuation-in-part application of U.S. application Serial No. 07/267,572, filed on November 7, 1988.

The title of the application is amended to more accurately reflect the claimed subject matter.

Amended claim 1 is supported, for example, by Tables 1 and 2 of the specification.

Support for the amendments to claim 22 may be found, for example, in originally-filed claim 4 and in the specification at page 11, line 26 through page 12, line 9.

New claims 23-27 are supported in Figures 3-8, 10-11, 15-16, 18, 24, and 26.

New claims 28-30 are supported at page 45, line 29 through page 46, line 5 and page 70, lines 1-24 of the specification.

In the Office Action dated September 17, 1993, the Examiner asserted that the claims as filed were directed to distinct inventions. The Examiner requested an election from the following groups of claims: the claims in Group I (claims 1-5) are directed to a 4-1BB cDNA; the claims in Group II (claims 6-8 and 17-20) are directed to a 4-1BB protein, e.g., produced by recombinant means, a 4-1BB fusion protein, and a method of using the fusion protein; the claims in Group III (claims 9-16) are directed to a 4-1BB extracellular domain-specific monoclonal antibody, a hybridoma which secretes the antibody, and methods of using the antibody to enhance T cell activation or proliferation; and the claim in Group IV (claim 21) is directed to a method of inducing B cell proliferation. Applicant elected, with traverse, the invention of Group I. It is Applicant's position that new claims 23-30 belong to the claims assigned to Group I as claims 28-30 are directed to DNA molecules encoding at least a portion of murine 4-1BB and claims 23-27 are dependent on claims 1 and 22.

In the final Office Action dated August 21, 1995, the Examiner rejected 1) claims 1-3 and 22 under 35 U.S.C. § 101; 2) claims 1-3 and 22 under 35 U.S.C. § 112, first paragraph; 3) claim 22 under 35 U.S.C. § 112, second paragraph; and 4) claims 1-3 and 22 under 35 U.S.C. § 102(b) as anticipated by Kwon et al. (Proc. Natl. Acad. Sci. USA, 86, 1963 (1989)). In the Examiner's Answer dated July 17, 1996, the rejection of claims 1-3 and 22 under 35 U.S.C. § 101 and claims 1-3 and 22 under 35 U.S.C. § 112, first paragraph, was withdrawn.

The 35 U.S.C. § 112, second paragraph, rejection

The Examiner rejected claim 22 under 35 U.S.C. § 112, second paragraph, asserting that it is not clear which compounds are claimed in subparagraph b). The amendments to claim 22 moot this rejection. It is respectfully submitted that the pending claims are in conformance with the requirements of § 112, second paragraph. Hence, the Examiner is respectfully requested to withdraw the § 112, second paragraph, rejection of claim 22.

The 35 U.S.C. § 102(b) rejection

The Examiner rejected claims 1-3 and 22 under 35 U.S.C. § 102(b) as being anticipated by Kwon et al. (Proc. Natl. Acad. Sci. USA, 86, 1963 (1989)). In particular, the Examiner asserts that claims 1-3 and 22 of the present application are not entitled to the filing date of the parent application, i.e., Serial No. 07/267,577, filed on November 7, 1988, as the '577 application allegedly fails to disclose how to use the claimed DNA in a manner that meets the requirements of 35 U.S.C. § 101 and § 112, first paragraph, and so Kwon et al. (1989) is prior art to the present application. This rejection is respectfully traversed.

Claims 1-3 and 22 are directed to a DNA encoding murine 4-1BB, including a portion of the DNA which specifically hybridizes to the DNA sequence shown in Figure 2 of the present specification or its complement. The '577 specification discloses that to isolate DNA encoding immune system-specific proteins, e.g., lymphokines, a differential screening method which employs at least two selection steps may be employed (page 2, lines 12-23 of the '577 specification). For example, a cDNA library prepared from a specific cell type may be screened with a probe prepared from RNA expressed in a different cell type and a "subtracted" probe

which represents RNA expressed in a desired cell type. Thus, to identify cDNA clones of T cell-specific genes, it is disclosed that a library, prepared from concanavalin A (ConA) stimulated T cells (L2 cells, a helper T cell line or L3 cells, a murine cytolytic T cell line), was screened with a probe prepared from RNA from a B cell line and another probe comprising cDNA from a T cell line (from L2 cells or L3 cells) from which sequences corresponding to B cell-specific RNAs had been eliminated ("subtracted") (pages 4-7 of the '577 specification). Using this method, DNA encoding murine 4-1BB was identified, isolated and sequenced.

The '577 specification also discloses that Northern blot analysis of various cell types with 4-1BB probes showed that 4-1BB RNA is expressed in both ConA-stimulated L2 and L3 cells but not in TPA-stimulated EL-4 cells (a murine thymoma line), K46 cells (a B cell lymphoma) or rat NK large granular lymphocytes ("LGL" cells) (see Figures 4, 6, and 8 of the '577 specification). It is also disclosed that 4-1BB RNA is found in L3 cells contacted with an anti-T cell receptor (TCR) antibody but not L3 cells stimulated with IL-2 (Figure 7), in L2 and CTL dB45 cells after TCR stimulation (Figure 8), in ConA-stimulated hybridomas (Figure 9), in an unstimulated CTL line (CTLLA11), and in ConA-stimulated murine splenocytes (Figure 11).

Hence, the '577 specification discloses that 4-1BB is expressed in T cells, and that its expression is induced by T cell activation (the mRNA is present in an "undetectable amount in T cells until induced by concanavalin A, or by TCR stimulation", see page 18, lines 17-19 of the '577 specification). Therefore, the '577 specification evidences a utility for the claimed DNA: as a probe to identify T cells, e.g., T helper cells, cytotoxic T cells, and activated T cells.

As Applicant has identified a specific utility for 4-1BB DNA and has indicated where support for the utility is found in the '577 specification (M.P.E.P. 706.03(a)(1), see section (B)(3)(i)-(ii) of the Guidelines for Examination of Applications for Compliance with the Utility Requirement of 35 U.S.C. § 101 and § 112), Applicant is entitled to claim the benefit of the filing date of the '577 application, i.e., November 7, 1988. Therefore, Kwon et al. is not 35 U.S.C. § 102(b) prior art to claims 1-3 and 22 of the present application. Hence, withdrawal of the rejection of the claims under § 102(b) is respectfully requested.

Conclusion

It is respectfully submitted that the claims are in condition for allowance and notification to that effect is respectfully requested. If any questions remain with respect to the present application, the Examiner is requested to contact Applicant's Representatives at the below-listed number.

Respectfully submitted,

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